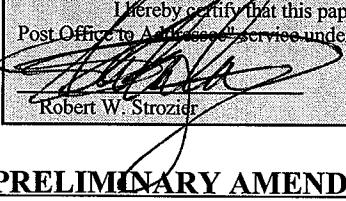


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: **HARDIN ET AL.** § ART UNIT NO.: **1633**
SERIAL NO.: **09/901,782** § EXAMINER: **SMITH, CL**
FILED: **7/9/2001** § DOCKET NO.: **00007/01UTL**
§
TITLE: **REAL-TIME SEQUENCE**
DETERMINATION §

571-273-8300	CERTIFICATE OF MAIL BY FACSIMILE TRANSMISSION	22 May 2007
FACSIMILE NO.		Date of Deposit
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 Robert W. Strozier		EXAMINER CL SMITH
		MS AMENDMENT
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		22 May 2007
		Date of Signature

PRELIMINARY AMENDMENTS AFTER RCE PRIOR TO EXAMINATION

Dear Examiner Smith:

Preliminary Statement

Applicants are submitting, via a Rule 131 declaration of Dr. Hardin, a redacted copy of a proposal prepared and submitted to a Federal Funding Agency prior to 17 May 2000, the filing date of the Korlach et al. non-provisional parent application, USSN 09572530, and, the proposal is, therefore, an antedating reference proving prior invention. In particular, Applicants draw the Examiner's attention to the aspects of beta and gamma labeling on nucleotides.

To expedite the Examiner's ability to evidence prior invention of the currently claims of this application, Applicants are also submitting a chart mapping disclosure in the proposal to claim limitations in the current claims. Although Applicants intend the chart to clearly show support in the proposal for each claim limitation of each current claim, Applicants have not exhaustively included all proposal material directed to each claim limitation in the chart, but have included numerous relevant proposal disclosures supporting each claim limitation of each current claim. See Appendix A.

Applicants believe that the proposal supports the claimed inventions set forth in the current claims. Applicants believe that the proposal inherently supports beta phosphate tagged monomers, because the document specifically discloses that the tag remains with the pyrophosphate so that a nascent DNA duplex is formed. There are only two phosphates in traditional deoxynucleotide triphosphates that satisfy this requirement, the β -phosphate and the γ -phosphate. The proposal clearly discloses that the tag remains with the release pyrophosphate moiety. The proposal also specifically states that dNTPs are to be prepared with base, sugar or phosphate tags. Rather than getting side tracked on whether the proposal expressly discloses beta, Applicants have opted to

cancel the beta specific claims set (claims 57-63), without prejudice, as claims directed to beta will be pursued in a pending continuation/divisional.

The proposal clearly supports sequencing where each dNTP type has a different tag designed to emit a different characteristic fluorescent signature during an incorporation cycle – before, during and/or after monomer incorporation.

For example, the proposal discloses tagged polymerases and a strategy for tagging the polymerase through cysteine, either naturally occurring or engineered via site specific mutagenesis, and a strategy for locating sites for cysteine mutagenesis so that enzyme function is not impaired.

The proposal also clearly supports polymerizing agents that do not have the ability to remove previously incorporated monomers – in the case of polymerases, lacking 3' to 5' exonuclease activity (proofreading).

The proposal clearly supports:

- The use of gamma tagged dNTPs or pyrophosphate moiety tagged dNTPs, both of which result in the tag being released upon monomer incorporation, in sequencing;
- The use of tagged polymerases lacking the ability to remove previously incorporated monomers in sequencing;
- The use of gamma tagged dNTPs or pyrophosphate moiety tagged dNTPs in combination with tagged polymerases in sequencing; and
- All other inventions set forth in the present claim set.

As previously argued, Applicants have been unable to find any support for either beta or gamma labeling in the Korlach et al. 1999 provisional patent application. Without support, and according to the MPEP, Korlach et al are not entitled to the filing date of the provisional application for claims related to beta and gamma labeling of dNTPs. MPEP § 706.02 Rejection on Prior Art [R-3] V. DETERMINING THE EFFECTIVE FILING DATE OF THE APPLICATION

(D) If the application properly claims benefit under 35 U.S.C. 119(e) to a provisional application, the effective filing date is the filing date of the provisional application for any claims which are fully supported under the first paragraph of 35 U.S.C. 112 by the provisional application.

This premise is discussed in the "Cautions" section of the United States Patent and Trademark Office's November 2, 2005 document entitled "Provisional Application for Patent" which states, "[i]t is recommended that the disclosure of the invention in the provisional application be as complete as possible. In order to obtain the benefit of the filing date of a provisional application the claimed subject matter in the later filed non-provisional application must have support in the

provisional application."

Therefore, as to beta or gamma labeled dNTPs, Korlach et al. is only entitled to the 17 May 2000 filing date, now antedated, and not the provisional filing date of 19 May 1999.

If the Examiner believes that support for either beta or gamma labeling does exist in the Korlach et al 1999 provisional application, Applicants respectfully request that the Examiner specifically point out such support in order to expedite resolution of this issue.